REMARKS

Claims 1-160 were pending. Upon entry of this amendment, claims 1, 21, and 157-161 will be pending. Accordingly, two (2) independent claims and six (6) dependent clains are pending.

This amendment cancels claims 2-20 and 22-156, replaces claims 1, 21, and 157-160 with correspondingly numbered claims, and adds new claim 161, support for which is found on page 38, lines 5-22 of the specification. No new matter has been added.

A version of the claims with markings to show where changes have been made appears in Appendix A at the end of this communication.

During a telephonic interview, the Examiner requested Applicants to re-provide pages 350-866 of the specification.

Accordingly, Applicants are pleased to provide the pages requested by the Examiner.

CONCLUSION

Allowance of claims 1, 21, and 157-161 is respectfully requested.

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Respectfully submitted,
Winn, et al.

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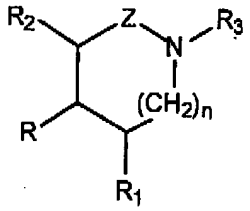
Appendix A
VERSION OF CLAIMS WITH MARKINGS TO SHOW CLANGES MADE
U.S. Application Ser. No. 09/653,563

1 (Amended). A compound of the formula:



wherein

Z is $-C(R_{18})(R_{19})-$ [or -C(O)-] wherein R_{18} and R_{19} are [independently selected from] hydrogen [and loweralkyl];

n is 0 [or 1];

R is $-(CH_2)_m-W$ wherein m is [an integer from] 0 [to 6] and W is

[(a)] $-C(O)_2-G$ wherein G is hydrogen [or a carboxy protecting group,

(b) $-PO_3H_2$,

(c) -P(O)(OH)E wherein E is hydrogen, loweralkyl or arylalkyl,

(d) -CN,

(e) $-C(O)NHR_{17}$ wherein R_{17} is loweralkyl,

(f) alkylaminocarbonyl,

(g) dialkylaminocarbonyl,

(h) tetrazolyl,

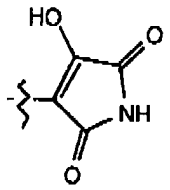
(i) hydroxy,

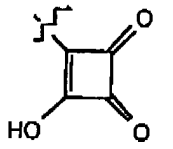
(j) alkoxy,

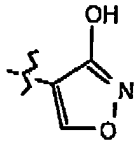
(k) sulfonamido,

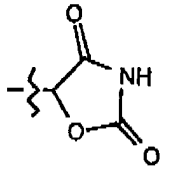
(l) $-C(O)NHS(O)_2R_{16}$ wherein R_{16} is loweralkyl, haloalkyl, aryl or dialkylamino,

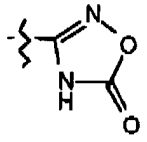
(m) $-S(O)_2NHC(O)R_{16}$ wherein R_{16} is defined as above,

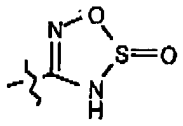
(n)  ,

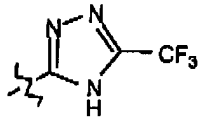
(o)  ,

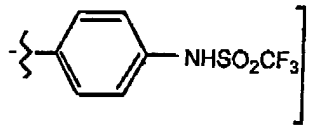
(p)  ,

(q)  ,

(r)  ,

(s)  ,

(t)  , or

(u)  ;

R_1 and R_2 are independently selected from **the group consisting of** [hydrogen,] loweralkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl,

haloalkyl, haloalkoxyalkyl, alkoxyalkoxyalkyl, thioalkoxyalkoxyalkyl, cycloalkyl, cycloalkylalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, aminocarbonylalkenyl, alkylaminocarbonylalkenyl, dialkylaminocarbonylalkenyl, hydroxyalkenyl, aryl, arylalkyl, aryloxyalkyl, arylalkoxyalkyl, (N-alkanoyl-N-alkyl)aminoalkyl, alkylsulfonylamidoalkyl, heterocyclic, (heterocyclic)alkyl and $(R_{aa})(R_{bb})N\text{-}R_{cc}$- wherein R_{aa} is aryl or arylalkyl, R_{bb} is hydrogen or alkanoyl and R_{cc} is alkylene[, with the proviso that one or both of R_1 and R_2 is other than hydrogen]; **and**

R_3 is [(a)] $R_4\text{-}C(O)\text{-}R_5$- [, $R_4\text{-}R_{5a}$-, $R_4\text{-}C(O)\text{-}R_5\text{-}N(R_6)$- , $R_6\text{-}S(O)_2\text{-}R_7$- or $R_{26}\text{-}S(O)\text{-}R_{27}$-]

wherein R_5 is [(i) a covalent bond, (ii)] alkylene[, (iii) alkenylene, (iv) $-N(R_{20})\text{-}R_8$- or $-R_{8a}\text{-}N(R_{20})\text{-}R_8$-

wherein R_8 and R_{8a} are independently selected from the group consisting of alkylene] and [alkenylene and

R_{20} is hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, cylcoalkyl or cycloalkylalkyl or

(v) $-O\text{-}R_9$- or $-R_{9a}\text{-}O\text{-}R_9$-

wherein R_9 and R_{9a} are independently selected from alkylene;

R_{5a} is (i) alkylene or (ii) alkenylene;

R_7 is (i) a covalent bond, (ii) alkylene, (iii) alkenylene or (iv) $-N(R_{21})\text{-}R_{10}$- or $-R_{10a}\text{-}N(R_{21})\text{-}R_{10}$-

wherein R_{10} and R_{10a} are independently selected from the group consisting of alkylene and alkenylene and R_{21} is hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl or arylalkyl;]

R_4 [and R_6 are independently] **is** selected from the group consisting of

(i) $(R_{11})(R_{12})N$- wherein R_{11} **is hydrogen** and R_{12} [are independently] **is** selected from **the group consisting of**

[(1) hydrogen,
(2) loweralkyl,
(3) haloalkyl,
(4) alkoxyalkyl,
(5) haloalkoxyalkyl,
(6) alkenyl,
(7) alkynyl,
(8) cycloalkyl,
(9) cycloalkylalkyl,
(10) aryl,
(11) heterocyclic,
(12)] arylalkyl,
[(13) (heterocyclic)alkyl,
(14) hydroxyalkyl,
(15) alkoxy,
(16) aminoalkyl,
(17) trialkylaminoalkyl,
(18) alkylaminoalkyl,
(19) dialkylaminoalkyl,] and
[(20) carboxyalkyl]
diarylalkyl

and

(ii) [loweralkyl,
(iii) alkenyl,
(iv) alkynyl,
(v) cycloalkyl,
(vi) cycloalkylalkyl,
(vii) aryl,
(viii) arylalkyl,
(ix) heterocyclic,
(x) (heterocyclic)alkyl,

(xi) alkoxyalkyl,

(xii) hydroxyalkyl,

(xiii) haloalkyl,

(xiv) haloalkenyl,

(xv) haloalkoxyalkyl,

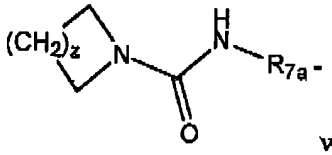
(xvi) haloalkoxy,

(xvii) alkoxyhaloalkyl,

(xviii) alkylaminoalkyl,

(xix) dialkylaminoalkyl,

(xx) alkoxy, and

(xxi)  wherein z is 0-5 and R_{7a} is alkylene;]

$(R_{11a})(R_{12a})N$-N(H)- wherein R_{11a} and R_{12a} are independently selected from the group consisting of aryl and alkyl

[R_{26} is (i) loweralkyl, (ii) haloalkyl, (iii) alkenyl, (iv) alkynyl, (v) cycloalkyl, (vi) cycloalkylalkyl, (vii) aryl, (viii) arylalkyl, (ix) heterocyclic, (x) (heterocyclic)alkyl, (xi) alkoxyalkyl or (xii) alkoxy-substituted haloalkyl; and

R_{27} is alkylene or alkenylene;

(b) R_{22}-O-C(O)-R_{23}- wherein R_{22} is a carboxy protecting group or heterocyclic and R_{23} is (i) a covalent bond, (ii) alkylene, (iii) alkenylene or (iv) -N(R_{24})-R_{25}- wherein R_{25} is alkylene and R_{24} is hydrogen or loweralkyl,

(c) loweralkyl,

(d) alkenyl,

(e) alkynyl,

(f) cycloalkyl,

(g) cycloalkylalkyl,

(h) aryl,

(i) arylalkyl,

(j) aryloxyalkyl,

(k) heterocyclic,

(l) (heterocyclic)alkyl,

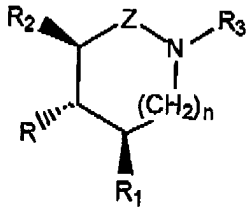
(m) alkoxyalkyl,

(n) alkoxyalkoxyalkyl, or

(o) R_{13}-C(O)-CH(R_{14})- wherein R_{13} is amino, alkylamino or dialkylamino and R_{14} is aryl or R_{15}-C(O)- wherein R_{15} is amino, alkylamino or dialkylamino];

or a pharmaceutically acceptable salt thereof.

21 (Amended). The compound according to [C]claim 1 of the formula:



[wherein

Z is -C(R_{18})(R_{19})- or -C(O)- wherein R_{18} and R_{19} are independently selected from hydrogen and loweralkyl;

n is 0 or 1;

R is -$(CH_2)_m$-W wherein m is an integer from 0 to 6 and W is

(a) -$C(O)_2$-G wherein G is hydrogen or a carboxy protecting group,

(b) -PO_3H_2,

(c) -P(O)(OH)E wherein E is hydrogen, loweralkyl or arylalkyl,

(d) -CN,

(e) -C(O)NHR_{17} wherein R_{17} is loweralkyl,

(f) alkylaminocarbonyl,

(g) dialkylaminocarbonyl,

(h) tetrazolyl,

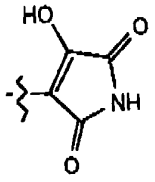
(i) hydroxy,

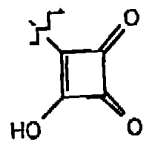
(j) alkoxy,

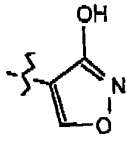
(k) sulfonamido,

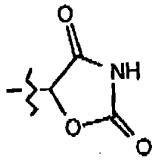
(l) -C(O)NHS(O)$_2$R16 wherein R16 is loweralkyl, haloalkyl, aryl or dialkylamino,

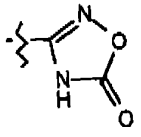
(m) -S(O)$_2$NHC(O)R16 wherein R$_{16}$ is defined as above,

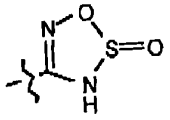
(n)  ,

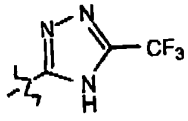
(o)  ,

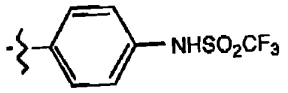
(p)  ,

(q)  ,

(r)  ,

(s)  ,

(t)  , or

(u) 

;

R_1 and R_2 are independently selected from hydrogen, loweralkyl, alkenyl, alkynyl, alkoxyalkyl, alkoxycarbonylalkyl, hydroxyalkyl, haloalkyl, haloalkoxyalkyl, alkoxyalkoxyalkyl, thioalkoxyalkoxyalkyl, cycloalkyl, cycloalkylalkyl, aminocarbonylalkyl, alkylaminocarbonylalkyl, dialkylaminocarbonylalkyl, aminocarbonylalkenyl, alkylaminocarbonylalkenyl, dialkylaminocarbonylalkenyl, hydroxyalkenyl, aryl, arylalkyl, aryloxyalkyl, arylalkoxyalkyl, (N-alkanoyl-N-alkyl)aminoalkyl, alkylsulfonylamidoalkyl, heterocyclic, (heterocyclic)alkyl and $(R_{aa})(R_{bb})N\text{-}R_{cc}$- wherein R_{aa} is aryl or arylalkyl, R_{bb} is hydrogen or alkanoyl and R_{cc} is alkylene, with the proviso that one or both of R_1 and R_2 is other than hydrogen;

R_3 is (a) $R_4\text{-}C(O)\text{-}R_5$-, $R_4\text{-}R_{5a}$-, $R_6\text{-}S(O)_2\text{-}R_7$- or $R_{26}\text{-}S(O)\text{-}R_{27}$-

wherein R_5 is (i) a covalent bond, (ii) alkylene, (iii) alkenylene, (iv) $-N(R_{20})\text{-}R_8$- or $-R_{8a}\text{-}N(R_{20})\text{-}R_8$-

wherein R_8 and R_{8a} are independently selected from the group consisting of alkylene and alkenylene and R_{20} is hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, cycloalkyl or cycloalkylalkyl or (v) $-O\text{-}R_9$- or $-R_{9a}\text{-}O\text{-}R_9$-

wherein R_9 and R_{9a} are independently selected from alkylene;

R_{5a} is (i) alkylene or (ii) alkenylene;

R_7 is (i) a covalent bond, (ii) alkylene, (iii) alkenylene or (iv) $-N(R_{21})\text{-}R_{10}$- or $-R_{10a}\text{-}N(R_{21})\text{-}R_{10}$-

wherein R_{10} and R_{10a} are independently selected from the group consisting of alkylene and alkenylene and R_{21} is hydrogen, loweralkyl, alkenyl, haloalkyl, alkoxyalkyl, haloalkoxyalkyl, aryl or arylalkyl;

R_4 and R_6 are independently selected from the group consisting of

(i) $(R_{11})(R_{12})N$- wherein R_{11} and R_{12} are independently selected from

(1) hydrogen,

(2) loweralkyl,

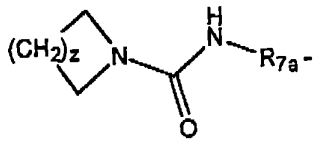
(3) haloalkyl,
(4) alkoxyalkyl,
(5) haloalkoxyalkyl,
(6) alkenyl,
(7) alkynyl,
(8) cycloalkyl,
(9) cycloalkylalkyl,
(10) aryl,
(11) heterocyclic,
(12) arylalkyl,
(13) (heterocyclic)alkyl,
(14) hydroxyalkyl,
(15) alkoxy,
(16) aminoalkyl, and
(17) trialkylaminoalkyl,

(ii) loweralkyl,
(iii) alkenyl,
(iv) alkynyl,
(v) cycloalkyl,
(vi) cycloalkylalkyl,
(vii) aryl,
(viii) arylalkyl,
(ix) heterocyclic,
(x) (heterocyclic)alkyl,
(xi) alkoxyalkyl,
(xii) hydroxyalkyl,
(xiii) haloalkyl,
(xiv) haloalkenyl,
(xv) haloalkoxyalkyl,
(xvi) haloalkoxy,
(xvii) alkoxyhaloalkyl,

(xviii) alkylaminoalkyl,

(xix) dialkylaminoalkyl,

(xx) alkoxy, and



(xxi)

wherein z is 0-5 and R_{7a} is alkylene;

R_{26} is (i) loweralkyl, (ii) haloalkyl, (iii) alkenyl, (iv) alkynyl, (v) cycloalkyl, (vi) cycloalkylalkyl, (vii) aryl, (viii) arylalkyl, (ix) heterocyclic, (x) (heterocyclic)alkyl, (xi) alkoxyalkyl or (xii) alkoxy-substituted haloalkyl; and

R_{27} is alkylene or alkenylene;

(b) R_{22}-O-C(O)-R_{23}- wherein R_{22} is a carboxy protecting group or heterocyclic and R_{23} is (i) a covalent bond, (ii) alkylene, (iii) alkenylene or (iv) -N(R_{24})-R_{25}- wherein R_{25} is alkylene and R_{24} is hydrogen or loweralkyl,

(c) loweralkyl,

(d) alkenyl,

(e) alkynyl,

(f) cycloalkyl,

(g) cycloalkylalkyl,

(h) aryl,

(i) arylalkyl,

(j) aryloxyalkyl,

(k) heterocyclic,

(l) (heterocyclic)alkyl,

(m) alkoxyalkyl,

(n) alkoxyalkoxyalkyl, or

(o) R_{13}-C(O)-CH(R_{14})-

wherein R_{13} is amino, alkylamino or dialkylamino and R_{14} is aryl or R_{15}-C(O)- wherein R_{15} is amino, alkylamino or dialkylamino;

or a pharmaceutically acceptable salt thereof].

157 (Amended). [A] **The** compound according to claim 1 [of formula (I)] wherein [n is zero; Z is -CH_2- wherein R_{18} and R_{19} are hydrogen; R is C(O)-G wherein G is hydrogen;] R_1 is aryl substituted with one substituent selected from **the group consisting of** methoxy, methoxyethoxy, and isopropoxyethoxy; R_2 is 1,3-benzodiox-5-yl; [R_3 is R_4-C(O)-R_5- wherein] R_5 is methylene; [and R_4 is selected from (R_{11})(R_{12})N-] and [(R_{11a})(R_{12a})N-N(H)-; one of R_{11} and] R_{12} is [hydrogen and the other is] selected from **the group consisting of** arylalkyl and diarylalkyl wherein each aryl group of the diarylalkyl is substituted with methyl or ethyl[; and one of R_{11a} or R_{12a} is alkyl and the other is aryl].

158 (Amended). [A] **The** compound according to claim 1 [of formula (I)] wherein [n is zero; Z is -CH_2- wherein R_{18} and R_{19} are hydrogen; R is C(O)-G wherein G is hydrogen;] R_1 is phenyl substituted with one substituent selected from **the group consisting of** methoxy, methoxyethoxy, and isopropoxyethoxy; R_2 is 1,3-benzodiox-5-yl; [R_3 is R_4-C(O)-R_5- wherein] R_5 is methylene; [and R_4 is selected from (R_{11})(R_{12})N-] and [(R_{11a})(R_{12a})N-N(H)-; one of R_{11} and] R_{12} is [hydrogen and the other is] selected from **the group consisting of** phenylalkyl and diphenylalkyl wherein each phenyl group of the diphenylalkyl is substituted with methyl or ethyl[; and one of R_{11a} or R_{12a} is alkyl and the other is phenyl].

159 (Amended). [A] **The** compound according to claim 21 [of formula (II)] wherein [n is zero; Z is -CH_2- wherein R_{18} and R_{19} are hydrogen; R is C(O)-G wherein G is hydrogen;] R_1 is aryl substituted with one substituent selected from **the group consisting of** methoxy, methoxyethoxy, and isopropoxyethoxy; R_2 is 1,3-benzodiox-5-yl; [R_3 is R_4-C(O)-R_5- wherein] R_5 is methylene; [and R_4 is selected from (R_{11})(R_{12})N-] and [(R_{11a})(R_{12a})N-N(H)-; one of R_{11} and] R_{12} is [hydrogen and the other is] selected from **the group consisting of** arylalkyl and

diarylalkyl wherein each aryl group of the diarylalkyl is substituted with methyl or ethyl[; and one of R_{11a} or R_{12a} is alkyl and the other is aryl].

160 (Amended). [A] **The** compound according to claim 21 [of formula (II)] wherein [n is zero; Z is $-CH_2-$ wherein R_{18} and R_{19} are hydrogen; R is C(O)-G wherein G is hydrogen;] R_1 is phenyl substituted with one substituent selected from **the group consisting of** methoxy, methoxyethoxy, and isopropoxyethoxy; R_2 is 1,3-benzodiox-5-yl; [R_3 is R_4-C(O)-R_5- wherein] R_5 is methylene; [and R_4 is selected from $(R_{11})(R_{12})N$-] and [$(R_{11a})(R_{12a})N$-N(H)-; one of R_{11} and] R_{12} is [hydrogen and the other is] selected from **the group consisting of** phenylalkyl and diphenylalkyl wherein each phenyl group of the diphenylalkyl is substituted with methyl or ethyl[; and one of R_{11a} or R_{12a} is alkyl and the other is phenyl].